the group consisting of T7, metallothionein I, and polyhedrin promoters.--

REMARKS

Applicants have studied the Office Action of April 20, 2000 ("Office Action"), and have made amendments to the claims. It is respectfully submitted that the application, as amended, is in condition for allowance. Claims 1-2, 5-11, and 19-38 are pending in the present application. The Applicant has amended claims 1-2, 5-9, 11, and 19, canceled claims 3 and 4, and added claims 20-38. No new matter has been added. Reconsideration and allowance of the claims in view of the above amendments and the ensuing remarks are respectfully requested. accession

The application as originally filed contained 23 claims (claims 1-23). In a response filed April 5, 2000 to a requirement for restriction, the Applicant elected to prosecute the claims of Group I, claims 1-11 and 19. In the Office Action dated April 20, 2000 ("Office Action") the Examiner withdrew the remaining claims, claims 12-18 and 20-23, as being drawn to a non-elected invention.

The Examiner objected in the Office Action that the title did not describe the invention to which the elected claims are directed. The Applicant has amended the title to "Nucleic Acids Encoding Transferrin Receptor-like Proteins" to more precisely describe the invention to which the pending claims are directed.

The Examiner objected to claims 1-11 and 19 as being indefinite under 35 U.S.C. § 112, first paragraph. The Examiner stated that "the specification, while being enabling for a nucleic acid encoding SEQ ID NO: 1, does not reasonably provide enablement for any other nucleic acid." Office Action, p. 2, ¶ 7. The Examiner further

objected that claims 1, 8, and 19 provide "no guidance as to what constitutes 'TfR2' polypeptide . . . The broad scope of claims 1, 8 and 19 can be read to encompass any isolated nucleic acid encoding a polypeptide."

The Applicant has amended claims 1, 8, and 19 such that they no longer recite "TfR2 polypeptide." Amended claims 1, 5, 8, and 19 are directed to nucleic acid and/or amino acid sequences defined with reference to the amino acid and/or nucleotide sequences disclosed in the specification (for example, SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3). Amended claim 1, for example, is directed to a nucleic acid molecule comprising a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 1;

(b) an amino acid sequence encoded by at least the nucleic acid sequence of SEQ ID NO: 2;

(c) an amino acid sequence encoded by at least the nucleic acid sequence of SEQ ID NO: 3.

(d) an amino acid sequence encoded by a nucleotide sequence having at least 60% homology with the nucleotide sequence of SEQ ID NO: 2;

(e) an amino acid sequence encoded by a nucleotide sequence having at least 60% homology with the nucleotide sequence of SEQ ID NO: 3;

(f) an amino acid sequence encoded by a nucleotide sequence that will hybridize under moderate stringency conditions to the nucleotide sequence of SEQ ID NO: 2; and

(g) an amino acid sequence encoded by a nucleotide sequence that will

hybridize under moderate stringency conditions to the nucleotide sequence of SEQ ID NO: 3

The specification describes several ways of obtaining such nucleic acids:

> DNA sequences of the invention can be obtained by several methods. For example, the DNA can be isolated using hybridization techniques well known in the art. These include, but are not limited to: 1) hybridization of genomic or cDNA libraries with probes to detect homologous nucleotide sequences, 2) polymerase chain reaction (PCR) on genomic DNA or cDNA using primers capable of annealing to the DNA sequence of interest, and 3) antibody screening of expression libraries to detect cloned DNA fragments with shared structural features. Specification, page 8, ¶ 2.

The specification provides several more examples at page 9, line 18 through page 10, line 19, all of which describe standard laboratory techniques.

The Applicant respectfully submits that the specification fully enables any one of ordinary skill in the art of microbiology to make and use the amino acid and nucleotide sequences of claims 1-11, and 19, as amended. On these grounds, the Applicant respectfully requests that the Examiner withdraw the objection under 35 U.S.C. § 112, second paragraph.

The Examiner further objected to claim 11 under 35 U.S.C. § 112, second paragraph, stating that the claim recites the term "capable of . . ." (the remaining portion of claim 11 recites "capable of specifically binding to and inhibiting the translation of mRNA of claim 9") and that "the specification is non-enabling for oligonucleotides that do not bind and inhibit translation of the mRNA of claim 9. . . ." The Applicant has

amended claim 11 so that it no longer recites the term "capable of." Claim 11, as amended, now recites "An anitisense oligonucleotide sufficiently complementary to the mRNA of claim 9 so as to inhibit its translation." The specification discusses such oligonucleotides at length at page 18, line 8 through page 19, line 10.

The Applicant respectfully submits that the specification fully enables any one of ordinary skill in the art of microbiology to make and use the oligonucleotide sequences of claim 11, as amended. On these grounds, the Applicant respectfully requests that the Examiner withdraw the objection under 35 U.S.C. § 112, second paragraph.

The Examiner objected to claims 1, 8 and 19 under 35 U.S.C. § 112, second paragraph, stating that "they only describe the peptide of interest by an arbitrary protein name." The Applicant has amended claims 1, 8, and 19 such that they no longer recite "TfR2 polypeptide." Instead, amended claims 1, 5, 8, and 19 are directed to nucleic acid and/or amino acid sequences defined with reference to the nucleic acid and/or amino acid sequences disclosed in the specification (for example, SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3).

The Applicant respectfully submits that claims 1, 5, 8 and 19 distinctly claim the amino acid and nucleotide sequences recited therein. On these grounds, the Applicant respectfully requests the Examiner to withdraw the objection under 35 U.S.C. § 112, second paragraph.

The Examiner further objected to claim 5 under 35 U.S.C. § 112, second paragraph, stating that it recites the term "'substantially,' which is a conditional term and renders the claim indefinite." The Applicant has amended claim 5 such that it no longer recites the term "substantially." Claim 5, as amended, is directed to an isolated nucleic

acid molecule comprising a nucleotide sequence selected from the group consisting of

(a) a nucleotide sequence having at least 60% homology with the nucleotide sequence of SEQ ID NO: 2;

(b) a nucleotide sequence having at least 60% homology with the nucleotide sequence of SEQ ID NO: 3;

(c) a nucleotide sequence that will hybridize under moderate stringency conditions to the nucleotide sequence of SEQ ID NO: 2;

(d) a nucleotide sequence that will hybridize under moderate stringency conditions to the nucleotide sequence of SEQ ID NO: 3.

One may find support for each of species a, b, c, and d in the specification at, for example, page 8, lines 10-15.

The Applicant respectfully submits that claim 5, as amended, distinctly claims the nucleic acid molecule recited therein. On these grounds, the Applicant respectfully requests that the Examiner withdraw the objection under 35 U.S.C. § 112, second paragraph.

The Examiner objected to claim 8 under 35 U.S.C. § 112, second paragraph, stating that it recites the term "'functional', which is a conditional term and renders the claim indefinite." The Applicant has amended claim 8 so that it no longer recites the term "functional." Claim 8, as amended, is directed to a host cell of claim 7, wherein the cell expresses a polypeptide having a sequence defined with reference to the amino acid and nucleotide sequences disclosed in the specification (for example, SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3).

The Applicant respectfully submits that claim 8, as amended, distinctly claims the

host cell recited therein. On these grounds, the Applicant respectfully requests that the Examiner withdraw the objection under 35 U.S.C. § 112, second paragraph.

The Examiner objected to claim 11 under 35 U.S.C. § 112, second paragraph, stating that it recites the term "'specifically binding', which is a conditional term which renders the claim indefinite." The Applicant has amended claim 11 so that it no longer recites the term "specifically binding." Claim 11, as amended, is directed to an anitisense oligonucleotide sufficiently complementary to the mRNA of claim 9 so as to inhibit its translation.

The Applicant respectfully submits that claim 11, as amended, distinctly claims the oligonucleotide recited therein. On these grounds, the Applicant respectfully requests that the Examiner withdraw the objection under 35 U.S.C. § 112, second paragraph.

The Examiner objected to claim 11 under 35 U.S.C. § 102(b) as being anticipated by Hiller et al. (1996). The Applicant respectfully traverses this objection.

Hiller et al. discuss the generation of 319,311 express sequence tags ("ESTs") recovered from random cDNA clones. The Examiner has cited to a sequence of mRNA ("Sequence Comparison A"), apparently identified by Hiller et al., which the Examiner states "would hybridize to the mRNA of claim 9, and inhibit translation."

Claim 11, as amended, is directed to an anitisense oligonucleotide sufficiently complementary to the mRNA of claim 9 so as to inhibit its translation. The mRNA of claim 9 comprises isolated mRNA complementary to the DNA of claim 2; the DNA of claim 2, in turn, comprises a nucleic acid molecule of claim 1, wherein the nucleic acid molecule comprises a molecule selected from the group consisting of DNA, cDNA, and

RNA.

Hiller et al. do not teach, disclose, or suggest a antisense oligonucleotide that is sufficiently complementary to the mRNA of claim 9 so as to inhibit its translation. Hiller et al. merely disclose a sequence (the Examiner has labeled this sequence "Sequence Comparison A") which they describe as "cDNA clone IMAGE:429423 5* similar to gb:M11507 TRANSFERRIN RECEPTOR PROTEIN (HUMAN)." There is nothing in the Hiller reference or in Sequence Comparison A itself that suggests that this sequence comprises an oligonucleotide that can both bind and inhibit the translation of the mRNA of claim 9, as required by claim 11, as amended.

> The entirety of the Examiner's objection under 35 U.S.C. § 102(b) is as follows: Claim 11 is rejected under 35 U.S.C. § 102(b) as being anticipated by Hiller et al. (1996). Hiller et al. discloses the cloning of an EST which would hybridize to the mRNA of claim 9, and inhibit translation. See Sequence Comparison A, attached.

The Applicant respectfully submits that this statement is by itself insufficient to establish a prima facie case of anticipation. It is the Examiner – and not the Applicant – that bears the burden of establishing a prima facie case of anticipation. Ex parte Levy, 17 U.S.P.Q.2d 1461, 1463-1464 (Bd. Pat. App. & Int. 1990) ("the initial burden of establishing a prima facie basis to deny patentability to a claimed invention rests upon the examiner."); Ex parte Kung, 17 U.S.P.Q.2d 1545, 1548 (Bd. Pat. App. & Int. 1989) ("even though the examiner bears a lesser burden of proof in making out a prima facie case of anticipation or obviousness, it remains upon the examiner to show that the [prior art substance] reasonably appears to be either identical with or only slightly

different that the claimed [substance]").

The Applicant respectfully submits that the Examiner cannot establish a prima facie case of anticipation by merely citing to an EST and stating, offering neither explanation nor evidence in support, that the EST meets all the limitations of claim 11, as amended. For this reason, the Applicant respectfully requests that the Examiner withdraw the objection under 35 U.S.C. § 102(b).

The Examiner objected to claim 19 under 35 U.S.C. § 103(a) as being unpatentable over Hiller et al. in view of Chonn et al. (1995). The Applicant respectfully traverses this objection.

The Examiner states that the "disclosure of Hiller et al. differs from the disclosed invention by not disclosing a composition of the antisense oligonucleotide in a hydrophobic carrier," but that "it would have been obvious . . . to use the liposomes of Chonn et al to deliver the antisense oligonucleotide of Hiller et al." Claim 19 is directed to an amount of the antisense oligonucleotide of claim 11 effective to modulate expression of at least a polypeptide of claim 1 and an acceptable hydrophobic carrier capable of passing through a cell membrane. As the Applicant has argued above, Hiller et al. does not teach, disclose, or suggest the antisense oligonucleotide of claim 11. Accordingly, the Applicant respectfully submits that Hiller et al., even when considered in view of Chonn et al., does not render claim 19 obvious. For this reason, the Applicant respectfully requests that the Examiner withdraw the objection under 35 U.S.C. § 103(a).

Applicant believes that the foregoing amendments place the application in condition for allowance, and respectfully requests early, favorable action on this

application.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call either of the undersigned attorneys at the Los Angeles telephone number (213) 488-7100 to discuss the steps necessary for placing the application in condition for allowance should the Examiner believe that such a telephone conference would advance prosecution of the application.

Respectfully submitted,

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Date: August 21, 2000

By: _____

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